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EDITORIAL COMMENT

The Shape of LVH in Hypertension

What Does it Tell Us?*

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Increased LV mass (actually weight) as well as the pattern of that increase has long been associated with adverse outcomes in patients with hypertension. Over one-half century ago, it was suggested that left ventricular hypertrophy (LVH) was a physiological adaptation to increased workload (1,2), and that the shape (geometry) assumed by the left ventricle (LV) as it hypertrophied depended on whether the work imposed on the LV was pressure or volume overload.

Specifically, in the presence of pressure overload, as occurs with hypertension, increased LV mass occurs with normal LV cavity volume but increased wall thickness (i.e., "concentric" LVH), whereas with volume overload, as occurs with mitral regurgitation, increased LV mass occurs with increased LV volume but normal wall thickness (i.e., "eccentric" LVH). The so-called eccentricity harkens back to roentgenographic evaluation of LVH, where the dilated LV is displaced leftward relative to its normal position in the chest (3). This basic categorization of LV geometry in patients with LVH had been further expanded (4–7) to include the division of eccentric LVH into dilated and nondilated forms, and a mixed (or concentric dilated) geometry with both increased wall thickness relative to cavity size and LV dilation.

Changes in LV geometry can be considered to be "adaptive" in that the increased wall thickness of concentric hypertrophy acts to normalize wall stress while the increased myocyte length in volume overload helps preserve stroke volume (8). These theoretical considerations aside, early echocardiographic studies (9) showed that concentric LVH in fact was associated with greater, not lesser, risk of death and morbidity than eccentric LVH, itself associated with increased risk. Moreover, even individuals with concentric remodeling defined as normal LV mass, but increased relative wall had increased risk of adverse events. However, geometric patterns of LVH are associated with differing risk factors, including the degree of increase in LV mass, and subsequent studies (10–12) with greater power and statistical adjustment for confounders suggested that LV geometry may not confer prognostic benefit independent of LV mass and traditional risk factors. Apart from the potential value of LV geometry to identify risk, LV geometry may be useful to predict treatment responses to antihypertensive treatment (13), and hypertension treatment may favorably alter LV geometry (14).

SEE PAGE 1034

In this issue of *iJACC*, Garg et al. (15) present data from 2,458 participants (31% hypertensive, 10% diabetic) in the Dallas Heart Study who underwent cardiac magnetic resonance (CMR) for assessment of LV mass and geometry. Participants were followed for a median of 9 years for the primary outcome of incident heart failure or death. Admirably, partition values for LV mass and geometry were internally derived from healthy study subjects within the Dallas Heart Study, and classification of LVH geometry was extended beyond previous methods.

Utilizing measured average wall thickness, LV diastolic volume, and computed concentricity (a measure of LV mass/volume ratio), the authors defined 4 categories of LVH and compared outcomes in these categories to the reference category of normal LV mass. Concentric remodeling was not defined or evaluated. The greatest risk for the combined endpoint of cardiovascular death or heart failure was in the 4% of participants with LVH who had dilated eccentric LVH, followed by the 1% with a mixed pattern of LVH characterized by both increased

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concentricity and LV dilation. In contrast, the risk of the combined endpoint did not achieve significance in the largest group of participants with LVH, that is, the 55% with indeterminate LVH (i.e., not meeting criteria for LV dilation or increased concentricity), and was modest in the 40% of participants with the thick-walled form of concentric LVH. These findings are consistent with those recently reported by investigators who applied the Dallas Heart Study classification of LVH to echocardiographic evaluation of an open hypertension registry of 8,848 subjects in Southern Italy (12).

The authors are to be congratulated for a carefully conducted study of a large and well-characterized population-based cohort using CMR, a more difficult but also a more accurate and reproducible technique for measurement of LV mass and presumably LV geometry than echocardiography, which is utilized in most clinical studies of LVH.

However, there are several caveats regarding the findings of this study. Even with a 9-year follow-up of a large cohort, the number of events (n = 81) was too low to separate incident heart failure from cardiovascular death. Given the relatively young age of the cohort at the time of study, a longer duration of follow-up would have been necessary to capture the maximum number of events, and the young age of the subjects challenges the generalizability of the findings to an older population with higher disease burden. The analyses did not include potential confounders, including LV mass and volume, that were unequally distributed across the risk gradient of geometric subtypes. Hence, it remains uncertain whether association of LV geometry with adverse outcomes is greater than simply using LV mass.

Importantly, the high-risk LVH subgroups only accounted for slightly less than one-half of events. The plurality of events (41%) occurred in the reference group with normal LV mass and normal geometry, and the majority of events occurred in structurally normal or low-risk groups. Hence, although the investigators identified geometric subgroups of individuals with LVH at particularly high relative risk, the actual prevalence of high-risk groups among those with LVH was low (e.g., mixed LVH only had 7 subjects). Hence, the population-attributable risk of cardiovascular death or heart failure in groups with high relative risk is low.

Nonetheless, the findings of this and other studies of cardiac end-organ response to hypertension are of great interest and reintroduce the long-standing hope that tailoring the treatment of hypertension to cardiac phenotype, in this case LVH and its geometric subtypes determined by CMR, could improve outcomes in those who are at high risk and avoid unnecessary treatment in those at low risk. However, this hypothesis has never been adequately tested.

One important limitation to the wider use of CMR is cost. In the United States alone, approximately 76.4 million adults have hypertension (16). At even the arguably modest current Medicare/Medicaid reimbursement for basic cardiac CMR of $356.61 (CPT code 35550), 1 study per patient with hypertension would cost over $27.3 billion, and the cost of sequential studies to monitor treatment effects would be truly astronomic.

As has been the case with the use of echocardiography in hypertension (17), the value of CMR will be difficult to establish. Moreover, existing strategies that are not guided by imaging for lowering blood pressure have been effective in reducing mortality and morbidity. Hence, it will be difficult to justify large-scale funding of randomized controlled trials designed to determine the practicability and efficacy of therapy targeted to cardiac structural phenotype. Nonetheless, the pathophysiological insights obtained from this and other studies of cardiac phenotypes in hypertension may help researchers to develop refined risk models that could be helpful, particularly if unnecessary treatment could be avoided in subgroups of patients with elevated blood pressure but low risk.

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